Dioxathion 393 1 - SEP 1978

I. Acute Toxicity.

Animal	Sex	Formulation	Route	LD_{50} or LCT_{50}
Rat, Sprague-Dawley	Male	Technical	Oral	43-45 mg/kg
Rat, Albino	?	Technical	Oral	111 mg/kg
Rat, Holtzman	Male	100% A.I.	Oral	50.1 mg/kg
Rat, Holtzman	Male	Technical	Oral	64 mg/kg
Rat, Glazo-Weston	Male	Technical	Oral	80 mg/kg
Rat, Glazo-Weston	Female	Technical	Oral	40 mg/kg
Rat, Sherman	Male	Technical	Oral	43 mg/kg
Rat, Sherman	Female	Technical	Oral	23 mg/kg
Mouse, Albino	?	Technical	Oral	176 mg/kg
Dog, Mongrel	Mixed	Technical	Oral	10-40 mg/kg
Rabbit, Albino	?	Technical	Dermal	0.08-0.09 cc/kg
Rabbit, Albino	?	2 lbs/gal	Dermal	0.32-0.36 cc/kg
Rabbit, Albino	?	4 lbs/gal	Dermal	0.16 cc/kg
Rabbit, Albino	?	4 lbs/gal	Dermal	145 mg/kg
Rat, Albino	?	Technical	Respiratory	Less than 20.9 (1 hr. LCT_{50})
Rat, Wistar	Mixed	Technical	Respiratory	1398 ug/l (LCT_{50})

* The LCT_{50} values are for dioxathion (diox) aerosols in the 2-u range.

Signs of toxicity were depression, diarrhea, salivation, lacrimation, exophthalmos, increased respiration, tremors, ataxia, and sprawling of limbs in rodents and dogs. Signs of toxicity in chickens were depression, ataxia reduced pain responses and an inability to break the fall when dropped to the floor. In all animals for which studies were reported, acute doses caused reductions in serum, erythrocyte, and brain cholinesterase (ChE) activities.

II. Irritation Studies.

One group of five rabbits was treated with undiluted technical diox and a second group of five rabbits with technical diox diluted to 25% in corn oil. All animals were treated by instilling 0.1 ml of the diox preparation into the eyes. Neither material produced eye irritation.

III. Subacute Toxicity.

Technical diox (5 mg/kg) was given orally to albino rats of both sexes for 21 days. Plasma, red blood cell (RBC), and brain ChE activities were 80, 73, and 91% (average of male and female animals), respectively, of controls after the first dose. Maximum inhibition of ChE activities in plasma (58%) in brain (58%) was noted on the 7th and 21st day after dosing, respectively. Maximum inhibition of brain ChE was greater in females (70%) than in males (46%).

A 90-day subacute study in albino weanling rats (Charles River strain) (25 of each sex) was conducted at dietary diox levels of 100 and 500 ppm. All of the animals in the high-dose group were sacrificed after 7 days because of food refusal and weight loss. Necropsy and histological examinations of these animals did not reveal any abnormalities or lesions that could be attributed to diox administration. Five males and five females in the low dose (100 ppm in the feed) group were sacrificed after 3, 6, 9, and 13 weeks of diox administration. Female rats exhibited signs of hyperexcitability and slight tremors; male rats did not exhibit any signs of toxicity. This dose of diox (100 ppm) did not cause mortality or produce any adverse effects on growth or food consumption. Necropsy and histological examinations of tissues did not reveal any diox-produced abnormalities or lesions.

Weanling albino rats (25 of each sex/treatment group) were given diox at dietary levels of 1, 3, and 10 ppm for up to 13 weeks. The animals in the 1, 3, and 10 ppm groups consumed 0.077, 0.22, and 0.78 mg/kg/day, respectively. The rats receiving 10 ppm diox had brain ChE activities which were not significantly different from control after 3, 6, 9, or 13 weeks of treatment but plasma and RBC ChE activities were signifcantly reduced at

these times. Animals receiving the lower doses (1 and 3 ppm) did not show any significant reduction in plasma, RBC, or brain ChE activity. Female and male animals gave similar results. Necropsy and histological examinations failed to reveal any abnormalities that could be related to ingestion of diox at the levels fed.

IV. Chronic Toxicity.

Reports dealing with studies on the chronic toxicity of diox have not been reported.

V. Oncogenicity.

No reports were found concerning the possible oncogenic effects of diox.

VI. Mutagenicity.

No reports were found concerning the possible mutagenic effects of diox.

VII. Teratology.

See the comments in section VIII (Reproductive Effects) of this report.

VIII. Reproductive Effects.

A three-generation study on the effects of diox (3 and 10 ppm in the feed) in Sprague-Dawley rats demonstrated that diox (3 or 10 ppm) -treated parental animals had normal growth patterns; neither treatment resulted in increased mortality nor were any unusual behavioral patterns observed. Liver weights and body: organ weight ratios were similar to those of controls. Administration of diox (3 or 10 ppm in the diet) produced no reproductive effects (measured as the mating index, fertility index, parturition index, mean litter size, live birth index, 5-day survival index, lactation index, and weanling body weights.

No evidence of teratogenicity was noted in any of the progeny in any generation.

These results indicate that a dietary level of 10 ppm diox may be considered a NOEL for reproductive effects in the rat.

IX. Neurotoxicity

Rhode Island Red chickens were given diox as single oral doses (10-1000 mg/kg) or single subcutaneous doses (25-200 mg/kg). Positive

controls, treated with a single oral dose of triorthocresol phosphate (500 mg/kg), developed neurological symptoms within 2 weeks of treatment. Diox-treated hens either died from an acute toxic dose or recovered without developing any signs of neurologic damage.

References

U.S. Environmental Protection Agency, Office of Pesticide Programs, Criteria and Evaluation Division, December, 1977. Initail Scientific Review of Dioxathion. Substitute Chemical Program. EPA-68-01-4198. Washington, D.C.

Gerald M. Marquardt, Ph.D.
Pharmacologist, Toxicology Branch
Hazard Evaluation Division

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